IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	Surmeier, et al.	Group No.:	1635
Serial No.:	10/761,557	Examiner:	Chong
Filed:	01/21/2004		
Entitled:	**Manipulation of Neuronal Ion Channels**		

SECOND DECLARATION OF D. JAMES SURMEIER, Ph.D. UNDER 37 CFR § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF TRANSMISSION UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being transmitted to the United States Patent and Trademark Office transmitted via the Office electronic filing system in accordance with 37 C.F.R. §1.6(a)(4).

Dated: May 13, 2009 By: /Michele R. Gilmer/
Michele R. Gilmer

Examiner Chong:

I, D. James Surmeier, Ph. D. hereby declare and state, under penalty of perjury, that:

1. I am one of the inventors of U.S. patent application 10/761,557 covering neuronal ion channels and manipulation of neuronal ion channels. I have worked in the field of physiology and have numerous publications in this field.

2. Prior to the present invention, there was very little work on Kv3.4 subunits because they appeared not to be important in determining the properties of Kv3 channels underlying fast spiking behavior.

3. For example, the Erisir et al. reference cited by the Examiner in the present Office Action states that the fast-spiking and rapid repolarization of the action potential was fully

explained by the properties of Kv3.1-2 subunits (See e.g., abstract). Additional references that explain the fast spiking properties of neurons without the inclusion of Kv3.4 include Macica et al. (J. Neurosci 21:1160 (2001); hereinafter Macica et al., 2001) and Macica et al. 2003 (J. Neurosci 23:1141 (2003); hereinafter Macica et al., 2003), both of which are attached hereto.

4. In 2003, prior to the present invention, there were no publications arguing that Kv3.4 subunits were important in spike repolarization in neurons; most of the interest in Kv3.4 subunits was focused on muscle, based upon the statement in the Weiser et al. reference cited by the Examiner in the present Office Action that the predominant expression of this channel was in muscle, not in the brain.

5. In addition to their predominant location in muscle, the role of Kv3.4 subunits in modulating the properties of Kv3 channels in neurons had been dismissed for two reasons. First, based on previously published work (Weiser et al. and Rudy et al., Ann N Y Acad Sci. 1999; hereinafter Rudy et al. and attached hereto), Kv3.4 channels were thought to inactivate rapidly, making it impossible for them to contribute to spike repolarization during high frequency repetitive discharge (as found in globus pallidus neurons). Heteromeric channels containing Kv3.4 and Kv3.1 subunits also were thought to rapidly inactivate (see Rudy et al). Experiments conducted during the course of development of the present invention showed that heteromeric channels containing a novel splice variant of Kv3.4 subunit (Kv3.4a) do not inactivate rapidly as previously shown for the Kv3.4b splice variant.

6. Second, based upon published work (Weiser et al, Rudy et al.), Kv3.4 containing channels were not capable of opening soon enough in an action potential to contribute in a significant way to spike repolarization. Experiments conducted during the course of development of the present invention and published shortly after the date of filing of the present application (Baranauskas et al., Nature Neuroscience 6:258 (2003); attached hereto) shows that this is only true of the Kv3.4b splice variant of Kv3.4 but not of the Kv3.4a splice variant that dominates channels in globus pallidus neurons. This splice variant shifts the voltage-dependence of Kv3.4 gating by 10-15 mV, allowing Kv3.4 containing channels to open soon after the beginning of a spike.

7. This was an unexpected and important finding, meriting its publication in Nature Neuroscience, one of the premier neuroscience journals in the world.

8. The results described in the present application were unexpected and contrary to the current state of the art and the time of filing of the present application.

9. I declare that all statements made herein are of my own knowledge and are true, and further that those statements are made with the knowledge that willful false statements and the like so mare are punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful, false statements may jeopardize the validity of the patent application or any patent issuing therefrom.

/D. James Surmeier/ /5/13/09

D. James Surmeier, Ph.D. Date